

Claims

1. An agent for inhibiting an excessive effect of NAD(P)H oxidase, which comprises a compound that does not substantially inhibit the effect of leukocyte NADPH oxidase but inhibits the
5 effect of NAD(P)H oxidase in a tissue other than leukocyte.

2. The agent of claim 1, wherein the tissue other than leukocyte is a tissue of a vascular cell, the heart, the kidney, the retina, the microglia or a tumor cell.

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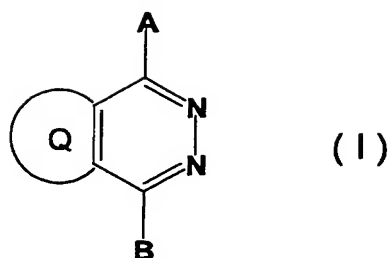
3. The agent of claim 1 or 2, wherein the excessive effect of NAD(P)H oxidase is caused by diabetes, hypertension, hyperlipidemia, obesity, smoking, heart failure, cardiac hypertrophy, ischemic heart diseases, angioplasty or ischemia-
15 reperfusion in organ transplantation.

4. The agent of claim 1 or 2, wherein the excessive effect of NAD(P)H oxidase is caused by cancer or dementia.

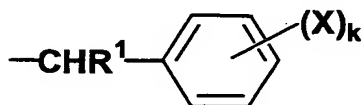
20 5. The agent of claim 1 or 2, wherein the excessive effect of NAD(P)H oxidase is caused by intake of chemicals.

6. The agent of any one of claims 1 to 5, wherein the compound that does not substantially affect leukocyte NADPH oxidase but
25 inhibits an excessive effect of NAD(P)H oxidase in a tissue other than leukocyte is a bicyclic pyridazine compound represented by the following formulas (I) to (VIII) or a pharmacologically acceptable salt thereof:

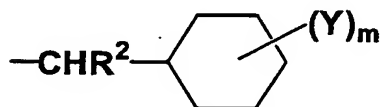
30 formula (I)



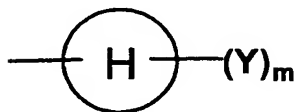
wherein A is C₃-C₆ alkyl, C₅-C₇ cycloalkyl, or phenyl, thienyl, furyl, thiazolyl, phenoxy, C₇-C₉ phenylalkyl, phenylthio, nitrogen-containing saturated ring group, pyridyl or imidazolyl,
 5 each optionally having one or more substituents selected from C₁-C₄ alkyl, C₁-C₄ alkoxy and halogen,
 B is -NH-D
 [D is



10 wherein R¹ is hydrogen or C₁-C₄ alkyl, X is halogen, C₁-C₄ alkyl or C₁-C₄ alkoxy, and k is an integer of 0 to 3, when k is an integer of 2 or more, multiple Xs may be the same or different,



15 wherein R² is hydrogen or C₁-C₄ alkyl, Y is C₁-C₄ alkyl or C₁-C₄ alkoxy, and m is an integer of 0 to 6, when m is 2 or more, multiple Ys may be the same or different, and any two Ys may be joined to form optionally branched C₁-C₆ alkylene,



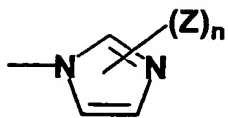
20 wherein ring H is C₅-C₇ cycloalkyl, and Y and m are as defined above,



wherein R³ is C₁-C₅ alkyl, and R⁴ is C₅-C₈ cycloalkyl or thienyl,

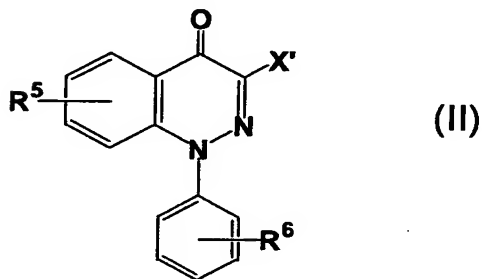
or C₃-C₈ alkyl]

or



wherein Z is C₁-C₄ alkyl or phenyl, and n is an integer of 0
5 to 2, when n is 2, these Zs may be the same or different, and
Q is a benzene ring, a furan ring or a thiophene ring
optionally substituted by C₁-C₄ alkyl,

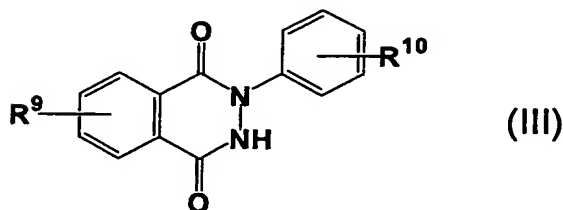
formula (II)



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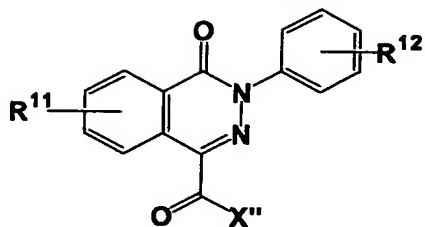
wherein R⁵ and R⁶ are each independently hydrogen, C₁-C₆ alkyl,
C₁-C₆ alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or
carboxyl, and X' is -COOR⁷ (R⁷ is hydrogen or optionally
substituted C₁-C₆ alkyl), -CONH₂, -CN, -COR⁸ (R⁸ is optionally
15 substituted C₁-C₆ alkyl or optionally substituted aryl), -NH₂,
-NO₂ or -OR⁷ (R⁷ is as defined above),

formula (III)

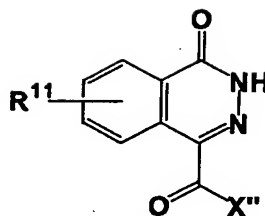


20 wherein R⁹ and R¹⁰ are each independently hydrogen, C₁-C₆
alkyl, C₁-C₆ alkoxy, halogen, cyano, nitro, amino,
trifluoromethyl or carboxyl,

formulas (IV) and (V)



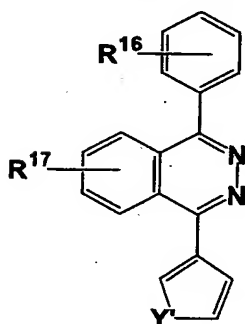
(IV)



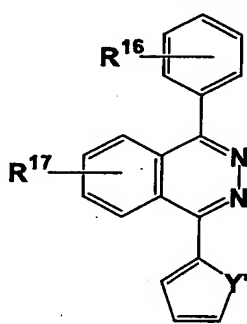
(V)

wherein R^{11} and R^{12} are each independently hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or
 5 carboxyl, and X'' is $-OR^{13}$ (R^{13} is hydrogen, C_1 - C_6 alkyl or aryl) or $-NR^{14}R^{15}$ (R^{14} and R^{15} are each independently hydrogen, C_1 - C_6 alkyl or aryl,

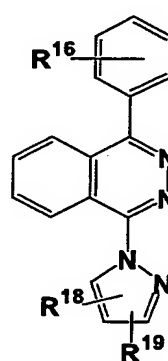
formulas (VI), (VII) and (VIII)



(VI)



(VII)



(VIII)

wherein R^{16} and R^{17} are each independently hydrogen, C_1 - C_6 alkyl, alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, R^{18} and R^{19} are each independently hydrogen or C_1 - C_6 alkyl, and Y' is oxygen or sulfur.

7. A pharmaceutical composition for the diseases caused by an excessive effect of NAD(P)H oxidase, which comprises the agent of any one of claims 1 to 6 as an active ingredient.

8. The pharmaceutical composition of claim 7, which is administered simultaneously with a hypolipidemic agent, an antihypertensive agent, a hypoglycemic agent, a vasodilator, an

antiplatelet agent, an anticoagulant, a brain protective agent, an anticancer agent, a diuretic agent, a cardiotonic agent, an analgesic agent, an antiedemic agent, a thrombolytic agent, an immunosuppressant, a steroid, a vitamin or an antioxidant, or
5 administered separately therefrom, or administered sequentially therewith.